

ORIGINAL ARTICLE

A Study on the Assessment of Correlation among Vitiligo and Dry Eye Diseases

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ABSTRACT

Objective: The aim of this research work was the assessment of the association of vitiligo disease and DED (Dry Eye Disease) with the help of different objective parameters.

Methodology: This research work was performed on 30 patients of vitiligo and 31 patients present with refractory complaints of non-complicated nature. Ophthalmologic examination was carried out on all the patients which included Schirmer Test-I, FBU (Fluorescein Break-up Time) and CFS (Cornea Fluorescein Staining). Different OSDI means (Ocular Surface Disease Index) were in utilization for the assessment of the dry eye status.

Results: Participants of both groups were same about the gender and age distribution. The patients of the vitiligo disease group were present with high scores of OSDI (24.10±13.70 versus 12.50±3.20, T-test, P<.0010), shorter FBU scores (5.6±2.7 versus 7.60±2.20, Mann's-Whitney U test, P=.0050) and higher positivity of CFS (18/30 versus 3/31, by Chi-square test, P<.0010) as related to the patients of control group. The patients of both groups were present with much similar results regarding the Schirmer and MGD outcomes. There was presence of peri-ocular involvement in 44.68% (n: 14) patients of vitiligo disease. Thorough analysis within the patients of vitiligo showed that the values of Schirmer test and FBU were much less in the patients present with peri-ocular involvement, MGD status and scores of OSDI were much similar.

Conclusion: This research work concluded that there is a possible correlation of vitiligo and DED. The tools of diagnosis for dry eye complication are in decent association with one another. For follow-up and diagnostic purposes, OSDI questionnaire seems much pragmatic.

Keywords: Metabolism, Dry Eye Disease, Hypochromic, Diagnosis, Refractory, Vitiligo.

INTRODUCTION

One of the most public subjects of daily practices in ophthalmology is the dry eye disease. Mostly, this disease is an isolated complication. But it can be present with some systematic disorders. This chronic condition may develop as an outcome of altered tear metabolism due to the dysfunction of the lacrimal functionality unit [1]. Vitiligo disease is a complication which can be categorized with the emergence of the hypochromic or achromic patches on mucous membrane as well as skin [2]. The description about the relationship of vitiligo with many other ocular diseases such as glaucoma, uveitis is available [3,4]. There is no available detail research work exploring the vitiligo with the dry eye disease. There is only one research work which interrogated this association and stated the alterations in the ocular tear and surface function [5]. The objective of this research work was to interrogate the presence of DED in the patients of vitiligo with the help of objective parameters and OSDI questionnaire and comparison of these findings with the subjects of the control groups.

METHODOLOGY

This study was conducted at Benazir Bhutto Shaheed Teaching Hospital Abbottabad and the duration this study was from March 2021 to July 2021. We took the written consent from all the patients of this study. There were 30 vitiligo patients in the study group & control group comprised of 31 patients. All the patients visited the Department of Ophthalmology suffering from refractory complaints of non-complicated nature. We excluded the

patients who were under active treatment of the vitiligo disease, patients with some ocular or systematic diseases or the patients who were on parenteral medication. Ophthalmologic examinations of all the patients were carried out including Schirmer Test-I, FBU (Fluorescein Break-up time) and CFS (Corneal Fluorescein Staining) under the impact of topical anesthesia.

We used the means of OSDI for the evaluation of the status of DED. The grading of the CFS staining was carried out in accordance with Oxford-scheme and severe nature of MGD (Meibomian Gland Dysfunction). Its classification was carried out affording the Bron's system [6]. Authors of this research study performed all the procedures. We recorded the data on standard sheet and SPSS V.21 program was used for the statistical analysis of the collected information.

RESULTS

Study-Group (group-V) & Control-Group (group-C) were much same about gender (Male to female ratio= 12:18 versus 12:19, by Chi-square test method, P=0.9180) and age distribution (41.28±10.8 versus 37.58±9.78 years, T-test, P=0.23). Scores of OSDI were high, shorter FBU and high positivity of CFS in the patients of vitiligo whereas the patients of groups were present with same regarding the results of Schirmer test and MGD status as presented in Table-1. There was presence of the peri-ocular involvement in 44.68% (n: 14) patients of vitiligo disease. When we investigated the patients of vitiligo disease regarding the involvement of periocular state, we found that the patients present with peri-ocular involvement were much less in age as compared to the patients who were

present without the peri-ocular involvement (37.58±10.88 years versus 44.48±8.68 years, T-test, P= 0.12).

Table 1: Comparison of Results of Two Groups (61 patients).

	Vitiligo (n= 30)		Control (n=31)		P value	
	Right eye	Left eye	Right eye	Left eye	Right eye	Left eye
FBU (seconds)	5.6±2.7	6.2±2.7	7.6±2.2	8±2.2	0.005a	0.003a
CFS * (0/1/2/3)	12/10/6/2	15/8/6/1	28/3/0/0	26/5/0/0	<0.001b	<0.005b
MGD * (1/2/3/4/5)	5/16/6/3/0	6/15/6/3/0	6/22/3/0/0	7/20/3/1/0	0.785b	0.806b
Schirmer test (mm)	7.6±2.4	8±2.7	9.2±3.2	9.4±3.1	0.055a	0.089a
OSDI score	24.1±13.7		12.5±3.2		<0.001c	

A Mann-Whitney U test, b: Chi-square test, c: t-test. comparison was done regarding absence versus presence status.

In the patients having vitiligo disease, FBU was much less than ten seconds in seventy percent for right-eye and seventy percent for left-eye when we got the comparison with the controls (46.38% for right-eye, by Chi-square test method, P=0.086 & 36.68% for left-eye, by Chi-square test

method, P= 0.014). Thorough examination of the different parameters of research work within the patients of vitiligo disease showed that there were shorter results of FBU and Schirmer tests in the patients present with the peri-ocular involvement, MGD status & scores of OSDI were same, the CFS availability was much prominent but insignificant statistically as presented in (Table-2).

Table 2: Comparison of Results Within Vitiligo Patients Regarding the Periocular (VPO+/-) Involvement (30 patients)

	Group VPO (+) (n= 14)		Group VPO (-) (n=16)		P value	
	Right eye	Left eye	Right eye	Left eye	Right eye	Left eye
FBU (seconds)	6.6±2.7	7.1±2.4	8.9±2.4	9.2±2.7	0.034a	0.052a
CFS * status (absent/present)	3/11	4/10	09/07	11/5	0.072b	0.066b
MGD* (absent/present)	2/12	3/11	3/13	3/13	1.000b	1.000b
Schirmer test (mm)	8.4±2.8	8.9±3.1	10.9±1.8	11.0±2.3	0.007a	0.043a
OSDI score	29.3±16.7		23.3±15.2		0.310c	

A Mann-Whitney U test, b: Chi-square test, c: t-test. comparison was done regarding absence versus presence status.

In this current research study, we spotted that there was correlation between the OSDI scores, Schirmer test, FBU and CFS with each other's excellently as showed in Table-3.

Table 3: The Correlations Between OSDI Scores and Other Objective Tests (61 patients)

	Correlation coefficient (Spearman's rho)	Significance (p value)
OSDI scores - FBU right eye	-0.508	<0.001
OSDI scores - FBU left eye	-0.503	<0.001
OSDI scores - CFS right eye	0.632	<0.001
OSDI scores - CFS left eye	0.629	<0.001
OSDI scores - Schirmer right eye	-0.349	0.006
OSDI scores - Schirmer left eye	-0.452	0.002

DISCUSSION

The prevalence of the vitiligo is 2.0% in the population and it is a significant disease of dermatology [7]. There is absence of any epidemiological research work on the occurrence of vitiligo. However, our national data on the basis of hospital registries stated prevalence of 1.40% among pediatrics [8] and 2.10% among population of adults [9]. This disease is chronic in nature and it needs regular treatment and complete follow-up. Another important topic of ophthalmologic practice is dry eye syndrome which has

a rate of prevalence of about 15.0% [10]. There is much lack in the data about the rate of prevalence of DED on national level. The information obtained with the use of a questionnaire by an epidemiological research work on Sjögren's Syndrome showed that 35.20% patients stated the complaints of persistent dry eye for greater than nineties days and 9.40% patients informed the regular usage of eye drops for tear substitution [11]. There is a vast study on the ophthalmologic consequences and most studied subject is uveitis due to its auto-immune inflammatory pathophysiology [12].

This current research work was carried out in order to interrogate this correlation, to rise the knowledge about the DED which damages the personal QoL and to evaluate OSDI tool's performance in this particular group of patients. There is dependency of the diagnosis of the DED on the grievances of patients and validation may be performed by the use of different objective parameters like Schirmer test, FBU and CFS. There are variable degrees of specificities and sensitivities of these tests [1]. In daily practices, questionnaires are essential in routine daily practices that comforts the process of diagnosis and evaluation of the treatment retort. There are different cut-off facts for such tools for diagnosis purpose. Since, outcome of the diagnostic tests of dry eye complication presents a comprehensive variability range among various conditions, dependent on that one single cut-off point has no reliability [13]. In a current research work, Alves stated that FBU and vital staining associated best with each other whereas the best combination of the test for the detection of the DED was OSDI, status of FBU and Schirmer [13]. The results of this research work also supported the same findings.

Facial involvement may be available up to 87% patients of vitiligo disease with various levels of severity [14]. There was presence of peri-ocular involvement in 60.0% patients. In our groups of the patients of vitiligo disease, 47% patients were present with peri-ocular involvement. It is revealed that there is an accumulation of the T-lymphocytes and apoptosis of melanocytes at the perilesional zones of vitiligo regions [15]. It is completely logical to forecast the ocular surface outcomes of vitiligo complication in the patients present with peri-ocular involvement. So, we performed an elaborate analysis in the patients present with the peri-ocular involvement. This research analysis in the patients of vitiligo disease showed that Schirmer rest and FBU were much less and there was more imminent CFS ($P=0.0720$ & $P=0.0660$) in the patients present with peri-ocular involvement whereas there were similar OSDI scores.

Most researched ocular complication in the patients of vitiligo disease was uveitis since last thirty years due to the possible common auto-immune pathophysiology [12]. In this research work, we excluded the patients who were present with well-established autoimmune or other systematic disease except vitiligo. We also excluded the patients of vitiligo who were under treatment since last one year. There are two types of categorizations of the dry eye disease which are tear deficiency and evaporative [1]. The leading reason of the evaporative type complication of DED is MGD [16]. In this current study, patients of both groups were similar in collaboration of the status of MGD. So, the non-availability of the MGD effect in the patients of our case group wires the dysfunction of lacrimal unit as a contributory feature which is the main reason in the tear metabolism. There are various probable factors of etiology underlying this dysfunction such as systematic autoimmune complications, age, environmental and hormonal factors, topical medications, surgery and wearing of contact lens which may all results the inflammatory dysfunction [17,18]. There is need of more detailed research works at the basic stage of inflammatory products in various groups of patients. This current study paves a way for various future works on different hints.

One significant outcomes of this research study are the usage of OSDI diagnostic tool in different patient groups present with dry eye disease. This is the 1st research study in whole literature which used the OSDI in the subjects of vitiligo disease. This research revealed that there is a good association of OSDI with some other diagnostic tools.

CONCLUSION

The findings of this research work suggest the correlation of vitiligo and DED. Different diagnostic tools for the disease of dry eye are in decent association with one another which has been confirmed in various groups of patients. For the follow-up purposes and diagnosis, OSDI questionnaire seems much pragmatic which can be used by the other medical disciplines.

REFERENCES

1. Karadag, R., Esmer, O., Karadag, A. S., Bilgili, S. G., Cakici, O., Demircan, Y. T., & Bayramlar, H. (2016). Evaluation of ocular

- findings in patients with vitiligo. *International Journal of Dermatology*, 55(3), 351-355.
2. Taheri, A. R., Allahyari, E., Rudi, B. H., & Nikandish, M. (2021). Dry Eye and Meibomian Glands in Vitiligo. *Turkish Journal of Ophthalmology*, 51(2), 70.
3. Arita, R., Fukuoka, S., & Morishige, N. (2017). New insights into the morphology and function of meibomian glands. *Experimental eye research*, 163, 64-71.
4. Fouad, Y. A., Salman, A. G., Mohamed, T. H., Abdelgawad, R. H. A., & Hassen, S. I. (2020). Assessment of the Effect of Vitiligo on Subfoveal Choroidal Thickness Using Spectral-Domain Optical Coherence Tomography. *Clinical Ophthalmology (Auckland, NZ)*, 14, 2265.
5. Yasar, E., Kemeriz, F., & Gurlevik, U. (2019). Evaluation of dry eye disease and meibomian gland dysfunction with meibography in seborrheic dermatitis. *Contact Lens and Anterior Eye*, 42(6), 675-678.
6. Wang, Q., Xie, X., Li, H., & Hao, S. (2020). Discovery of microRNA expression profiles involved in regulating TGF- β 2 expression in the tears of dry eye patients. *Annals of Clinical Biochemistry*, 57(6), 420-428.
7. Ozulken, K., Aksoy Aydemir, G., Tekin, K., & Mumcuoğlu, T. (2020, January). Correlation of non-invasive tear break-up time with tear osmolarity and other invasive tear function tests. In *Seminars in Ophthalmology (Vol. 35, No. 1, pp. 78-85)*. Taylor & Francis.
8. Galor, A., Feuer, W., Lee, D. J., Florez, H., Carter, D., Pouyeh, B., ... & Perez, V. L. (2011). Prevalence and risk factors of dry eye syndrome in a United States veterans affairs population. *American journal of ophthalmology*, 152(3), 377-384.
9. Senel E, DoğruerŞenel S, Salmanoğlu M. Prevalence of skin diseases in civilian and military population in a Turkish military hospital in the central Black Sea region. *J R Army Med Corps*. 2014 Aug 4. pii: jramc-2014-000267. doi: 10.1136/jramc-2014-000267.
10. Paulsen AJ, Cruickshanks KJ, Fischer ME, Huang GH, Klein BE, Klein R, et al. Dry eye in the beaver dam offspring study: prevalence, risk factors, and health-related quality of life. *Am J Ophthalmol*. 2014;157(4):799-806. DOI: 10.1016/j.ajo.2013.12.023
11. Birlık M, Akar S, Gurler O, Sari I, Birlık B, Sarioglu S, et al. Prevalence of primary Sjogrens syndrome in Turkey: a population-based epidemiological study. *Int J Clin Pract*. 2009;63(6):954-961. doi: 10.1111/j.1742-1241.2008.01749.x.
12. Greco A, Fusconi M, Gallo A, Turchetta R, Marinelli C, Macri GF, et al. Vogt-Koyanagi-Harada syndrome. *Autoimmun Rev*. 2013;12(11):1033-1038. DOI: 10.1016/j.autrev.2013.01.004
13. Alves M, Reinach PS, Paula JS, Vellasco e Cruz AA, Bachellet L, Faustino J, et al. Comparison of diagnostic tests in distinct well-defined conditions related to dry eye disease. *PLoS One*. 2014;9(5):e97921. DOI: 10.1371/journal.pone.0097921
14. Prabha, N., Chhabra, N., Shrivastava, A. K., Arora, R. D., Roja, V. R., Kaushik, S., & Nagarkar, N. M. (2019). Ocular abnormalities in vitiligo patients: A cross-sectional study. *Indian Dermatology Online Journal*, 10(6), 731.
15. Campanati, A., Neri, P., Giuliadori, K., Arapi, I., Carbonari, G., Borioni, E., ... & Offidani, A. (2015). Psoriasis beyond the skin surface: a pilot study on the ocular involvement. *International Ophthalmology*, 35(3), 331-340.
16. Dahir, A. M., & Thomsen, S. F. (2018). Comorbidities in vitiligo: comprehensive review. *International journal of dermatology*, 57(10), 1157-1164.
17. Lemp MA. Advances in understanding and managing dry eye disease. *Am J Ophthalmol*. 2008;146(3):350-356.
18. Fleissig, E., Pavlovksy, M., Loewenstein, A., Zur, D., Newman, H., Keren, S., ... & Goldstein, M. (2018). Prevalence of choroidal nevus and retinal pigment epithelial alterations in vitiligo patients. *Graefe's Archive for Clinical and Experimental Ophthalmology*, 256(5), 927-933.